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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,598	10/25/2001	David J. Hammond	92053/32	4545

7590 10/02/2003

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EXAMINER	
FALK, ANNE MARIE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,598	HAMMOND ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30,42 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply* .

DETAILED ACTION

The preliminary amendment filed October 25, 2001 has been entered. Claims 31-41 have been cancelled.

Claims 1-30, 42, and 43 are pending in the instant application and are examined herein.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Sequences are disclosed in the specification that are not identified by their sequence identifier (i.e., SEQ ID NO:). For example, at page 1, paragraph [0001] of the specification, an amino acid sequence is disclosed but is not identified by its sequence identifier. **Applicant is reminded that the entire specification and figures should be reviewed for sequence disclosures** and that each sequence disclosed in the specification must be identified by its sequence identifier (i.e., SEQ ID NO:). The specification must be amended to identify all disclosed sequences by their sequence identifier (i.e., SEQ ID NO), in accordance with 37 CFR 1.821(d).

Applicant is given the same shortened statutory period set forth for response to this Office Action within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of

time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Drawings

The drawings are objected to because Figures 1, 3, and 5A are of poor quality; the background is too dark and the features referred to in the specification are not visible. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a).

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout prosecution. All original claims must be numbered consecutively. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claim previously presented (whether entered or not).

The original claims include two claims numbered as Claim 22. The second instance of Claim 22 has been renumbered as Claim 23. Misnumbered Claims 23-42 have been renumbered 24-43, respectively.

Applicants are responsible for correcting the claim dependencies as appropriate.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 1-30, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of detecting the presence of prion protein in a sample, a method of isolating prion protein from a sample, a prion protein detection kit, a method for diagnosing a disease condition caused by an infectious prion protein, a method for screening for an agent which binds to the amino acid sequence Gln-Pro-His, and a method of screening for an agent that binds to two or more prion proteins.

The claims recite "an agent which binds to the amino acid sequence Gln-Pro-His of prion protein." However, the specification only discloses a single agent that binds to the amino acid sequence Gln-Pro-His, namely steptavidin. The agent is an essential element of the claimed invention, but the specification does not describe a representative number of species of agents that bind to the amino acid sequence Gln-Pro-His. Thus, one of skill in the art could not envision the entire genus of agents that bind to the amino acid sequence Gln-Pro-His and consequently, the written description requirement has not been met. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only a single agent, streptavidin, has been described by its complete structure. However, the claims cover the use of a genus of agents that bind to the amino acid sequence Gln-Pro-His. Next then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In this case, no other species have been described by other relevant identifying characteristics, such as a core structure responsible for the recited binding function.

This limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of agents other than streptavidin that bind to the amino acid sequence Gln-Pro-His, at the time the application was filed. Thus, it is concluded that the written description requirement is not satisfied for the genus of agents recited in the claims.

Enablement

Claims 26-30 and 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 26-30 are directed to a method for diagnosing a disease condition caused by an infectious prion protein.

In the event that the instant grounds of rejection were overcome, Claims 26-30 and 42 would still be subject to the scope of enablement rejection set forth below, wherein the only agent enabled for use in the method of detecting is streptavidin.

With regard to Claims 26-30, the specification fails to provide an enabling disclosure for the method for diagnosing a disease condition caused by an infectious prion protein because the detection method disclosed in the specification, wherein streptavidin is contacted with the sample being tested, does not distinguish the infectious form of prion protein from the non-infectious cellular form, PrP^{C}. The specification teaches that both PrP^{C} and PrP^{SC} bind to streptavidin as a result of the presence of the Gln-Pro-His amino acid sequence in both forms of the protein. Thus, there is no methodology disclosed for **specifically** detecting an **infectious** prion protein.

Claim 42 is directed to a method for screening for an agent which binds to the amino acid sequence Gln-Pro-His of the human prion protein by detecting the presence of the agent bound to the prion protein.

With regard to Claim 42, the specification fails to provide an enabling disclosure for the claimed screening method because no guidance is offered for selecting compounds that would be likely to have the desired binding properties. The screening method is nothing more than trial and error experimentation to identify compounds with the desired properties from amongst all compounds known to man. The screening assay involves taking any compound and testing it for binding to prion protein. Then at some point, presumably the specificity of the binding also must be tested, though the screening assay does not include a step for doing this. No guidance is offered for the requisite methodology for detecting the agent bound to the prion protein. The methodology for detecting agent-prion protein complex is highly dependent on the type of compound being tested. Since the agent is selected from any and all compounds known to man, there is no common assay for carrying out the detection step to thereby detect any and all agent-prion protein complexes. No guidance is offered for determining the specificity of the interaction of agent with prion protein. This is a critical step in identifying an appropriate agent. Given the lack of guidance with regard to the above-mentioned parameters, the screening method clearly would require the skilled artisan to engage in undue experimentation.

Claims 1-3, 8-13, and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting the presence of prion protein in a sample and a method of isolating prion protein in a sample by contacting the sample with **streptavidin** and detecting or isolating the streptavidin-prion protein complex, does not reasonably provide enablement for the methods of detecting and isolating prion protein by contacting the sample with any agent that binds to the amino acid sequence Gln-Pro-His of prion protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method of detecting the presence of prion protein in a sample.

The specification fails to provide an enabling disclosure for the methods of detecting and isolating prion protein by contacting a test sample with any agent that binds to the amino acid sequence Gln-Pro-His of prion protein because the specification only discloses one agent (streptavidin) that specifically binds to this amino acid sequence and furthermore does not offer adequate guidance for identifying other agents that specifically bind to this amino acid sequence. The specification suggests that a screening assay may be set up, but this screening assay is nothing more than trial and error screening of any compound known to man. The screening assay involves taking any compound and testing it for binding to prion protein. No guidance is offered for the requisite methodology for detecting the agent bound to the prion protein. The methodology for detecting agent-prion protein complex is highly dependent on the type of compound being tested. Thus, there is no common assay for detecting any and all agent-prion protein complexes. Furthermore, the binding interaction must be specific, but the specification does not offer any guidance for determining the specificity of the interaction. There are obviously many agents that will bind to any protein, including those that contain the Gln-Pro-His amino acid sequence. For example, Coomassie Brilliant Blue R stain binds to virtually any protein. The specification does not offer any guidance or direction for selecting appropriate compounds to test and therefore leaves the skilled artisan with nothing more than trial and error for testing any and all compounds. This would clearly require undue experimentation.

The specification fails to provide an enabling disclosure for the methods of detecting and isolating prion protein by contacting a test sample with any agent that binds to the amino acid sequence Gln-Pro-His of prion protein because the claim does not require that the agent **specifically** bind to the amino acid sequence. The claims encompass methods of using **any** agent that binds to the recited amino acid sequence, but detection can only be achieved when the agent is specific for the recited sequence (i.e. the agent does not also bind nonspecifically to other random proteins not desired to be detected).

Given the state of the art at the time of the invention, the lack of working examples directed to the selection of appropriate compounds that may specifically bind prion protein, the lack of guidance for

identifying agents that specifically bind to the amino acid sequence Gln-Pro-His of prion protein, and the undeveloped and unpredictable state of the art with respect to selecting agents that specifically bind to a particular protein, undue experimentation would have been required for one skilled in the art to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-7, 9, 10, 13-17, 24-30, 42, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-7 and 14-17 are indefinite in their recitation of "wherein the protein is streptavidin" because it is unclear whether the claim is intended to be limited to the embodiment wherein the **agent** is also streptavidin. In fact, the claim as written does not require that agent be limited to streptavidin because in Claim 3 or Claim 13 "the agent is a protein, peptide, polypeptide, nucleic acid, non-peptide organic molecule or organic reagent." Thus, the agent is still selected from amongst any of these classes of compounds, except that the protein can only be streptavidin. The claim language is confusing. The metes and bounds of the claim are not clearly set forth.

Claims 3-7 and 13-17 are indefinite in their recitation of "protein" or "polypeptide" because it is unclear how a protein would differ from a polypeptide. These terms are not defined in the specification in a manner such that they constitute distinct species. The terms should either be distinguished from each other or acknowledged as equivalents.

Claims 9 and 10 are indefinite because the order of the steps recited in the claims are not clearly set forth. Claim 9 is directed to the method of Claim 1, wherein the prion protein is detected by electrophoretic separation on a denaturing gel. Claim 1 involves contacting a test sample with an agent which binds to the amino acid sequence Gln-Pro-His of prion protein and detecting the agent bound to the

prion protein. This is confusing because Claim 1 only involves detecting agent-prion protein complexes but Claim 9 involves detecting prion protein alone. Furthermore it is unclear whether the detection by electrophoresis is the only method of detection or if there are two methods of detection, one that detects the agent bound to the prion protein and another one that just detects the prion protein.

Claims 16 and 24 are indefinite because improper Markush terminology is used. The claims recite "**or** a radiolabeled marker." Proper Markush group terminology requires the use of "and" rather than "or."

Claim 24 is indefinite in its recitation of "wherein the detectable marker is selected from ..." because the term "detectable marker" lacks antecedent basis in Claim 22.

Claim 25 is indefinite in its recitation of "wherein the enzyme is phosphatase" because "the enzyme" lacks antecedent basis in Claim 23.

Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: there is no step for interpreting the assay results to determine the diagnosis. The claim is directed to a method for diagnosing a disease condition caused by an infectious prion protein, but the final step is the detection of a complex between the prion protein and the agent. No diagnosis is determined as a result of said detection or lack of said detection.

Claims 27, 28, and 30 are indefinite in their recitation of "[t]he method of Claim 25" because Claim 25 is directed to a kit, not a method.

Claim 29 is indefinite in its recitation of "[t]he method of Claim 27" because Claim 27 is directed to "[t]he method of Claim 25" but Claim 25 is directed to a kit, not a method.

Claim 29 is indefinite because the agent is not limited to streptavidin and it is unclear whether the claim is intended to limit the agent to streptavidin. Claim 29 depends from Claim 28 which recites that "the agent is a protein, peptide, polypeptide, nucleic acid, non-peptide organic molecule or an organic reagent." However, only the **protein** is limited to streptavidin. The **agent** is still selected from any class

of compound recited in the group. The claim language is confusing. The metes and bounds of the claim are not clearly set forth.

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: contacting the agent with something, either purified prion protein, a peptide containing the Gln-Pro-His sequence, a sample containing prion protein, etc. The skilled artisan would not be able to detect agent bound to prion protein without doing something first to cause them to come into contact with each other and bind to each other. Claim 42 is missing another essential step because it does not include a step for determining the specificity of the binding interaction. One skilled in the art would recognize that an agent that binds non-specifically is useless.

Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step for determining whether the test agent actually binds to both prion proteins. The final step involves comparing the resulting levels of infectious and non-infectious prion protein to the initial levels combined.

Claim 43 is indefinite because it is unclear whether the "resulting levels of infectious and non-infectious prion protein" refers to free protein, complexed protein, or total protein. Furthermore, it is unclear whether the infectious and non-infectious prion proteins of the mixture are both from the same species of animal.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-25 are rejected under 35 U.S.C. 102(b) as being anticipated by the Calbiochem Biochemical and Immunochemical Catalog (1996), at pages 327 and 441.

The claims are directed to a prion protein detectable kit comprising an agent which binds to the amino acid sequence Gln-Pro-His of prion protein.

The Calbiochem Biochemical and Immunochemical Catalog (1996) discloses on pages 327 and 441 streptavidin-enzyme conjugates and streptavidin-fluorophore conjugates known in the prior art. Applicant is reminded that the intended use for a composition in a kit carries no patentable weight. The prion protein binding properties are an inherent property of streptavidin. Discovery of a new property or use of a previously known composition, even if unobvious from the prior art, cannot impart patentability to claims to a known composition (see *In re Spada*, 15 USPQ2d 1655, CAFC 1990).

Thus, the claimed composition is disclosed in the prior art.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to William Phillips whose telephone number is (703) 305-3482.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER